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vessel. The oily vehicle may be any oily vehicle described herein, for example, Capmul MCM.

Step **104** comprises mixing Gelucire 44/14 with the oily vehicle. Mixing may be facilitated by an impellor, agitator, or other suitable means. Step **102** may be performed under an inert or relatively inert gas atmosphere, such as nitrogen gas N₂. Mixing may be performed in any suitable vessel, such as a stainless steel vessel.

Step **106** comprises mixing estradiol into the mixture of the oily vehicle and Gelucire 44/14. Mixing may occur in a steel tank or vat. Mixing may be facilitated by an impellor, agitator, or other suitable means. Step **106** may be performed under an inert or relatively inert gas atmosphere, such as nitrogen gas N₂.

Step **108** comprises cooling to room temperature. Cooling may be allowed to occur without intervention or cooling may be aided by application of a cooling system.

Step **110** comprises mixing micronized progesterone into the mixture of oily vehicle, estradiol and Gelucire 44/14. Mixing may occur in a steel tank or vat. Mixing may be facilitated by an impellor, agitator, or other suitable means. Step **110** may be performed under an inert or relatively inert gas atmosphere, such as nitrogen gas N₂. Step **112** comprises degassing. The resulting mixture from step **112** may comprise a fill material suitable for production into a softgel capsule.

With reference to FIG. 2, softgel capsule, i.e. gel mass, production **200** is shown. Step **202** comprises mixing glycerin with water. The water used in step **202** may be purified by any suitable means, such as reverse osmosis, ozonation, filtration (e.g., through a carbon column) or the like. Mixing may be facilitated by an impellor, agitator, or other suitable means. Step **202** may be performed under an inert or relatively inert gas atmosphere, such as nitrogen gas N₂. Heating may be performed until the temperature reaches 80° C.±5° C.

Step **204** comprises the addition of gelatin to the glycerin water mixture. Mixing may be facilitated by an impellor, agitator, or other suitable means. Step **204** may be performed under an inert or relatively inert gas atmosphere, such as nitrogen gas N₂. A vacuum may be drawn in step **204** to de-aerate.

Step **206** comprises addition of a coloring agent such as a dye. A coloring agent may comprise products sold under the trademark OPATINT or other suitable agent. Step **206** may be performed under an inert or relatively inert gas atmosphere, such as nitrogen gas N₂. Step **208** comprises degassing. The resulting mixture from step **208** may comprise a gel capsule material suitable for use as a gel capsule in production of a softgel capsule.

With reference to FIG. 3, softgel capsule assembly process **300** is shown. Step **302** comprises heating the fill material. The fill material may be heated to any suitable temperature. In various embodiments, the fill material is heated to 30° C.+/-3° C. Fill material may be heated in a fill hopper. A fill hopper may comprise a device configured to hold a volume of the fill material and/or to dispense the fill material in controlled volumes.

Step **304** comprises filling a gel mass. A gel mass may be taken from the gel capsule material produced in step **208** of FIG. 2. Filling may be performed by injecting, placing, or otherwise disposing the fill material within a volume defined by the gel capsule material. The filling may occur in an encapsulator. The spreader boxes may be a temperature of 55° C.+/-10° C. The wedge temperature may be 38° C.+/-3° C. The drum cooling temperature may be 4° C.+/-2° C. The encapsulator may be lubricated using MIGLYOL 812 or other suitable lubricant. Step **304** thus produces one or more softgel capsules. Filling may comprise producing a ribbon of thick-

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ness 0.85 mm±0.05 mm using spreader box knobs. The fill material may be injected into the gel to produce a fill weight having target weight ±5% (i.e., 650±33 mg and 325±16.3 mg).

Step **306** comprises drying the softgel capsules. Drying may be performed in a tumble dryer, tray dryer, or combinations thereof. For example, drying may be performed in a tumble drying basket for between about 10 minutes and about 120 minutes. Drying may continue in a drying room for about 24 hours to about 72 hours. Step **308** may comprise inspection and/or polishing. Polishing may be performed with isopropyl alcohol. Step **310** may comprise packaging. Packaging may be accomplished through any suitable means. Packaging may comprise packing softgel capsules into a blister pack, bottle, box, pouch, or other acceptable packaging.

What is claimed is:

1. A pharmaceutical composition comprising:

solubilized estradiol;
suspended progesterone; and
a solubilizing agent;

wherein each of the estradiol and the suspended progesterone are present in the solubilizing agent and the estradiol and progesterone are uniformly dispersed;
wherein at least about 90% of the estradiol is solubilized in the solubilizing agent; and

wherein the solubilizing agent comprises an effective amount of a monoglyceride, a diglyceride or a combination thereof containing an ester of a C6-C12 fatty acid.

2. The pharmaceutical composition of claim 1, further comprising partially solubilized progesterone, wherein the partially solubilized progesterone is solubilized in the solubilizing agent.

3. The pharmaceutical composition of claim 1, wherein the formulation is formulated as a gelatin capsule.

4. The pharmaceutical composition of claim 1, wherein said estradiol has a dosage strength of at least about 0.125 mg and wherein said progesterone has a dosage strength of at least about 25 mg.

5. The pharmaceutical composition of claim 1, wherein the ratio of progesterone to estradiol is about 24:1, about 25:1, about 96:1, about 100:1, about 192:1, or about 200:1.

6. The pharmaceutical composition of claim 1, wherein the estradiol does not precipitate for at least 14 days.

7. A pharmaceutical composition comprising:

solubilized estradiol;
suspended progesterone; and
a solubilizing agent;

wherein each of the estradiol and the suspended progesterone are present in the solubilizing agent and the estradiol and progesterone are uniformly dispersed;
wherein at least about 90% of the estradiol is solubilized in the solubilizing agent; and

wherein the solubilizing agent comprises an effective amount of a monoglyceride thereof containing an ester of a C6-C12 fatty acid.

8. The pharmaceutical composition of claim 7, further comprising partially solubilized progesterone, wherein the partially solubilized progesterone is solubilized in the solubilizing agent.

9. The pharmaceutical composition of claim 7, wherein the composition is formulated as a gelatin capsule.

10. The pharmaceutical composition of claim 7, wherein the estradiol has a dosage strength of at least about 0.125 mg and wherein the progesterone has a dosage strength of at least about 25 mg.